The scientific abstract.

Critical limb ischemia (CLI) is the most serious presentation of peripheral arterial disease (PAD) which over 10 million patients in the United States. CLI manifests as rest pain, tissue loss (ulcers and gangrene), and the risk of limb amputation. Currently, the most widely used method for diagnosing CLI in patients involves measuring the ankle-brachial index (ABI) and clinical symptoms of the patient. Growth factors, such as vascular endothelial growth factor (VEGF-A), have been shown in animal studies to improve blood flow to the lower limbs by promoting the growth of new blood vessels.

Study #0310-611 entitled "Modulation of Vascular Endothelial Growth Factor (VEGF) Using an Engineered Zinc-finger transcription Factor to Treat Lower Limb Intermittent Claudication" was positively reviewed by RAC, the FDA, the NIH IRB, and IBC; and is under way at the NHLBI. It was designed to establish the safety and tolerability of transcriptional upregulation of the isoforms of VEGF-A in patients with intermittent claudication of intramuscular administration of EW-A-401. EW-A-401 contains a plasmid formulated in neutral copolymer which expresses a zinc finger transcription factor engineered to enhance the production of all VEGF-A isoforms. To date, no serious adverse events have been reported in this study.

Similar to the above-mentioned study, this study is designed to measure the safety and tolerability of EW-A-401 in patients with critical limb ischemia (CLI). This study is an open label, dose escalation, repeated dose design. In addition, we will collect exploratory efficacy and biological activity data including perfusion, function, quality of life, and evaluate progenitor cell populations in the treated subject.